

UNITED STATES DEPARTMENT OF COMMERCE United States Patent and Trademark Office Address COMMISSIONER FOR PATENTS PO Box 1450 Alcassedan, Virginia 22313-1450 www.emplo.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,194	06/30/2005	Bertus Noordam	GRT/4662-45	8070
23117 7590 04/10/2009 NIXON & VANDERHYE, PC			EXAMINER	
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ARLINGTON	, VA 22203		ART UNIT	PAPER NUMBER
			1623	
			MAIL DATE	DELIVERY MODE
			04/10/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

The MAILING DATE of this communication appears on the cover sheet with the correspondence address Period for Reply	
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAY WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION. Extensions of time may be available under the provisions of 37 CFR 1.38(g), in no event, however, may a reply be timely filed after 5X (g) MONTHS from the mailing date of this communication. Failure to reply within the set or extended period for reply will, by statute, cause the supplication to become MAMOND-EC (38 U.SC. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patter them adjustments. See 37 CFR 1.74(b).	
Status	
1)⊠ Responsive to communication(s) filed on 30 Jan 2009 and 02 Feb 2009.	
2a) This action is FINAL . 2b) This action is non-final.	
3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits	is
closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11, 453 O.G. 213.	
Disposition of Claims	
4)⊠ Claim(s) 6-15 and 20-30 is/are pending in the application.	
4a) Of the above claim(s) is/are withdrawn from consideration.	
5) Claim(s) is/are allowed.	
6)⊠ Claim(s) <u>6-15 and 20-30</u> is/are rejected.	
7) Claim(s) is/are objected to.	
8) Claim(s) are subject to restriction and/or election requirement.	
Application Papers	
9) The specification is objected to by the Examiner.	
10) The drawing(s) filed on is/are: a) accepted or b) objected to by the Examiner.	
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).	
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.12	1(d)
11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.	
Priority under 35 U.S.C. § 119	
12)⊠ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a)⊠ All b)□ Some * c)□ None of:	
 Certified copies of the priority documents have been received. 	
Certified copies of the priority documents have been received in Application No	
3. Copies of the certified copies of the priority documents have been received in this National Stage	
application from the International Bureau (PCT Rule 17.2(a)).	
* See the attached detailed Office action for a list of the certified copies not received.	

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DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on 30 Jan 2009 and 02 Feb 2009 have been entered.

This Office Action is responsive to Applicant's Amendment and Remarks, filed 30 Jan 2009, in which claims 6, 20 and 30 are amended to change the scope and breadth of the claim; and Applicant's Amendment and Remarks, filed 02 Feb 2009, in which claim 10 is amended to correct minor informalities.

This application is the national stage entry of PCT/EP04/00658, filed 23 Jan 2004; and claims benefit of foreign priority document EPO 03075255.4, filed 27 Jan 2003. The foreign priority document is in English.

Claims 6-15 and 20-30 are pending in the current application.

Rejections Withdrawn

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Applicant's Amendment, filed 30 Jan 2009 and 02 Feb 2009, with respect to rejection of claims 6, 8-13 and 20-30 rejected under 35 U.S.C. 103(a) as being unpatentable over Tanekawa et al. (US Patent 4,303,680, issued 1 Dec 1981, of record) in view of Keller et al. (US Patent 4,623,723, issued 18 Nov 1986, of record), with evidence provided by Kanegae et al. (US Patent 4,810,509, issued 7 Mar 1989, of record) and Chae et al. (Bioresource Technology, 2001, 76, p253-258, of record), has been fully considered and is persuasive with regard to instant claims 12 and 30, because Tanekawa et al. in view of Keller et al. does not specifically teach separating the RNA present in the released cell contents from other soluble cell material smaller than 50 kDa carried out by ultrafiltration with a filter as required by instant claim 12 and 30 and the provided evidence does not show this process to be necessarily present in the teaching of Tanekawa et al. in view of Keller et al.

This rejection of claims 12 and 30 has been **withdrawn**. This rejection of claims 6.8-11.13 and 20-29 is modified and reiterated below.

The following are new grounds of rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended Claims 12 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanekawa et al. (US Patent 4,303,680, issued 1 Dec 1981, of record) in view of Keller et al. (US Patent 4,623,723, issued 18 Nov 1986, of record) as applied to claims 6, 8-11, 13 and 20-29 in the modified rejection reiterated below, and further in view of Fernandez et al. (Acta Biotechnol., 1992, 12(1), p49-56, cited in PTO-892).

Tanekawa et al. in view of Keller et al. teaches as recited in the modified rejection reiterated below. Keller et al. teaches separating the RNA present in the aqueous cell extract, or released cell contents, by precipitating the RNA from the filtered permeate (column 2, lines 60-65), implicitly separating the RNA from other soluble cell material smaller than 50 kDa by the process of precipitation.

Tanekawa et al. in view of Keller et al. does not specifically teach separating the RNA present in the released cell contents from other soluble cell material smaller than 50 kDa by ultrafiltration with a filter and the RNA is recovered in the filter's retentate (instant claim 12). Tanekawa et al. does not specifically teach separating the RNA

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present in the released cell contents from other soluble cell material smaller than 50 kDa by ultrafiltration by a filter having a molecular weight cut-off from 10 kD to 50 kD (instant claim 30).

Fernandez et al. teaches separation by precipitation and ultrafiltration are known in the prior art as equivalent processes for the same purpose of purification of intracellular components, and teaches ultrafiltration is advantageous because avoids high temperatures or physicochemical changes that may alter the desired properties (page 49, paragraph 1 of Introduction). Fernandez et al. teaches concentrating and purifying RNA from cell extracts containing nucleic acids (page 49, paragraph 3 of Introduction) by ultrafiltration with hollow fiber membranes PM-10 and PM-30, or a filter having a molecular weight cut off of 10 or 30 kDa (page 50, paragraph 1 of section Ultrafiltration and paragraphs 1 and 2 of section Membrane Selection), implicitly separating the RNA present in the released cell contents from other soluble cell material smaller than 10 or 30 kDa for recovery in the retentate.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Tanekawa et al., in view of Keller et al. and further in view of Fernandez et al. All of Tanekawa et al., Keller et al. and Fernandez et al. are drawn to the separation of RNA from cell extracts containing nucleic acids. Fernandez et al. teaches separation by precipitation and ultrafiltration are known in the prior art as equivalent processes for the same purpose of purification of intracellular components. One of ordinary skill in the art would be motivated to substitute the separation by precipitation taught by Keller et al. for the separation by ultrafiltration taught by

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Fernandez et al. because Fernandez et al. teaches ultrafiltration is advantageous because avoids high temperatures or physicochemical changes that may alter the desired properties.

The following modified grounds of rejection are reiterated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended Claims 6, 8-11 and 13 and 20-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanekawa et al. (US Patent 4,303,680, issued 1 Dec 1981, of record) in view of Keller et al. (US Patent 4,623,723, issued 18 Nov 1986, of record),

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with evidence provided by Kanegae et al. (US Patent 4,810,509, issued 7 Mar 1989, of record) and Chae et al. (Bioresource Technology, 2001, 76, p253-258, of record).

Tanekawa et al. discloses a process for producing a flavoring composition containing 5'-ribonucleotides (column 2, lines 9-10) comprising (i) treating yeast cells to release cell contents comprising RNA (column 2, lines 13-16), (ii) extracting the RNA present in the released cell contents (column 2, lines 18-20), and (iii) converting the separated RNA into 5'-ribonucleotides (column 2, lines 21-25), meeting limitations of instant claim 6. Tanekawa et al. discloses treating the yeast cells to release cell contents comprising RNA by autolysis or hydrolysis using enzymes is a conventional method (column 1, lines 25-30), and Kanegae et al. explains that autolysis involves the action of proteases (Kanegae et al., column 3, line 39), meeting limitations of instant claims 8, 9 and 25. Tanekawa et al. discloses removal of insoluble solid material originating from the cells by methods such as centrifugation and filtration after extraction of RNA from the cell and prior to converting the separated RNA into 5'-ribonucleotides (column 4, lines 13-18), meeting limitations of instant claims 10 and 11. Tanekawa et al. discloses using a 5'-phosphodiesterase to hydrolyze the separated RNA into 5'nucleotides (column 4, lines 19-20) as well as deaminase (column 4, line 25), meeting limitations of instant claims 13, 26 and 27. Tanekawa et al. discloses the preferred yeast cells are Saccharomyces cerevisiae (column 3, lines 4-5), meeting limitations of instant claims 28 and 29. Tanekawa et al. discloses an example in which the composition produced comprises more 5'-GMP (0.78%) than the sum of 5'-IMP and 5'-AMP, enzymatically converted to 5'-IMP (0.7 %) (column 7, lines 38-40), meeting

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limitations of instant claim 24. Tanekawa et al. is silent as to the glutamate content of the yeast extract. Chae et al. explains that yeast extract prepared by a combination of protease, 5'-phosphodiesterase, and deaminase inherently contains 25.9% amino acids on a solid weight basis (Chae et al. page 257, left column, lines 26-29 and 33-35), and the amino acids composition is 7.80% glutamic acid (Chae et al. page 257, right column, table 3, entry "Glutamic acid"), giving a composition that comprises 2.02% w/w of glutamate, meeting limitations of instant claim 23.

Tanekawa et al. does not specifically disclose separating the RNA present in the released cell contents from other soluble cell material smaller than 50 kDa (instant claim 6 and 20, step (ii)) in the process of extracting the RNA present in the released cell contents (column 2, lines 13-16). Tanekawa et al. does not specifically disclose the removal of solid material originating from the cells prior to separating the RNA present in the released cell contents from other soluble cell material (instant claims 10 and 11). Tanekawa et al. does not disclose the process wherein the composition comprises at least 55% w/w of 5'-ribonucleotides (instant claim 20), at least 65% w/w of 5'-ribonucleotides (instant claim 21), or at least 75% w/w of 5'-ribonucleotides (instant claim 22).

Keller et al. teaches aqueous cell extracts containing nucleic acids (Keller et al. column 1, lines 5-17), corresponding to the RNA extract disclosed by Tanekawa et al. Keller et al. teaches separating the RNA present in the aqueous cell extract, or released cell contents, by precipitating the RNA from the filtered permeate (column 2, lines 60-65), implicitly separating the RNA from other soluble cell material smaller than 50 kDa

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by the process of precipitation. Example 8 in US Patent 4,206,243, referred to in Keller et al. column 2, lines 53-55 and excerpted here:

EXAMPLE &

Candida lipolytica ATCC 20383, a hydrocarbon-utiliizing yeast species, was quitivated on n-paraffins in the presence of an aqueous nutrient medium and an oxygencontaining gas. The yeast cell mass was senerated from the autrient solution and deled.

100 g of the dry yeast cell mass were suspended at room temperature under normal pressure in 300 g of methanol and 10 g of gaseous NH3 were added to this mixture within 15 minutes, the temperature of the suspension being maintained at 15' C. by cooling. After the 30 gas was introduced, agitation was continued for another 20 minutes at 22° C., followed by filtration through a suction frit. The filter cake was mixed once thoroughly on the frit with 300 ml of methanol, then vacuum filtered. The two flittates were combined. The solution 35 had a yellow color and contained the lipids of the originaily used cell material. Methanol and NH; were removed under reduced pressure (14 mm Hg).

The residue after the second filtration, consisting of the destroyed and degressed cells of the microorgan-so ism, was dried in a vacuum drying cabinet (100 mm Hg) at 40° C. for 5 hours. The thus obtained product exhibited a light color than the yeast cell mass originally

used, and was odorless.

100 g of degressed and dried yeast were suspended in 45 a solution of 1 liter of distilled water and 1000 ml of methanol, in order to reduce the original aucleic sold content of 7.5 weight %, calculated on the starting material. The mixture was agitated and, at a pH of 6.3 to which it adjusted itself, was heated to 50° C. for 15 so minutes. Then by centrifugation it was separated into a sediment containing the yeast protein, and a liquid phase containing nucleic acid. The sediment was subjusted to vacuum freeze drying after having been washed once more at room temperature.

The nucleic acid content of the dry material had diminished from the original 7.5 weight % to 0.4 weight

teaches the removal of solid material originating from the cells prior to the filtration taught by Keller et al., addressing instant claims 10 and 11. Keller et al. further teaches the isolation of the RNA (Keller et al. column 2, lines 45-49) to give a composition that is 100% 5'-ribonucleotides, meeting limitations of instant claims 20-22. Keller et al. also teaches the enzymatic degradation of the RNA-containing permeate without isolation to give the 5'-ribonucleotides (Keller et al. column 2, lines 3-8). Keller

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et al. teaches 5'-ribonucleotides used as foodstuff additives are obtained by treating the aqueous cell extracts containing nucleic acids with 5'-phosphodiesterase, and that the 5'-deoxynucleotides by-products produced by DNA reacting with 5'-phosphodiesterase are difficult to separate from the desired 5'-ribonucleotides (Keller et al. column 1, lines 18-27). Keller teaches "The exclusion limit of the membrane is selected to accord with the known or determined molecular weights of the nucleic acids to be separated" (column 1, lines 50-55) and that "Membrane separating processes are generally familiar and especially so in biotechnology" (column 1, lines 55-60).

It would have been obvious to one of ordinary skill in the art at the time of the invention to improve the process for producing a flavoring composition containing 5'-ribonucleotides disclosed by Tanekawa et al. with the known method taught by Keller et al. of separating the RNA present in the released cell contents from other soluble cell material. Both Tanekawa et al. and Keller et al. disclose production of 5'-ribonucleotides as a foodstuff additive, and Keller et al. teaches that it is desirable that the process be improved by separating the RNA present in the released cell contents from other soluble cell material prior to converting the separated RNA into 5'-ribonucleotides (Keller et al. column 1. lines 18-27).

Response to Applicant's Remarks:

Applicant's Remarks, filed 30 Jan 2009 and 02 Feb 2009, have been fully considered and found not to be persuasive with respect to instant claims 6, 8-11 and 13 and 20-29.

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Applicant notes that the separation by filtration taught by Tanekawa et al. in view of Keller et al. would not separate RNA from other soluble cell material smaller than 50 kDa. However, the limitation of separation of RNA from other soluble cell material smaller than 50 kDa by filtration is not found in instant claims 6, 8-11 and 13 and 20-29. but rather this limitation is found in instant claims 12 and 30. Regarding step (ii) of amended claims 6 and 20, Keller et al. teaches separating the RNA present in the aqueous cell extract, or released cell contents, by precipitating the RNA from the filtered permeate (column 2, lines 60-65), implicitly separating the RNA from other soluble cell material smaller than 50 kDa by the process of precipitation. The method taught by Tanekawa et al. in view of Keller et al., involving separation of the RNA by precipitation implicitly separates the RNA from other soluble cell material smaller than 50 kDa. rendering the instantly invention as claimed obvious, as step (ii) of amended claims 6 and 20 do not limit the method of separation.

One of ordinary skill in the art would have a reasonable expectation of success in separating the RNA from other soluble cell material smaller than 50 kDa by the process of precipitation because the process of precipitation is routinely used one of skill in the art to separate a desired precipitate from other soluble material.

Claim 6, 7 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanekawa et al. (US Patent 4,303,680, issued 1 Dec 1981, of record) in view of Keller et al. (US Patent 4,623,723, issued 18 Nov 1986, of record) as applied to claims

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6, 8-11, 13 and 20-29 above, and further in view of Potman et al. (US Patent 5,288,509, issued 22 Feb 1994, of record).

Tanekawa et al. in view of Keller et al. render unpatentable a process for producing a flavoring composition containing 5'-ribonucleotides (column 2, lines 9-10) comprising (i) treating yeast cells to release cell contents comprising RNA (Tanekawa et al. column 2, lines 13-16), (ii) separating the RNA present in the released cell contents from other soluble cell material (Keller et al. column 2, lines 58-65), and (iii) converting the separated RNA into 5'-ribonucleotides (Tanekawa et al. column 2, lines 21-25).

Tanekawa et al. in view of Keller et al. does not disclose the process wherein the native enzymes of the cell are inactivated prior to treating the cells to release the cell contents (instant claim 7).

Potman et al. teaches the process for preparing a yeast extract useful as a food flavor (Potman et al., abstract), involving the deactivation of the native enzymes of the yeast (Potman et al. column 2, lines 32-36) prior to the enzymatic degradation of the cell with a protease such as papain (Potman et al. example 1 on column 5, lines 6-14).

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute functional equivalent methods of enzymatic degradation of the cell to practice the invention of Tanekawa et al. in view of Keller et al. with the method involving the deactivation of the native enzymes of the yeast prior to the enzymatic degradation of the cell with an exogenous protease such as papain taught by Potman et al. in place of autolysis with the cell's endogenous protease with a reasonable expectation of success. Tanekawa et al. discloses treating the yeast cells to release

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cell contents comprising RNA by autolysis or hydrolysis using enzymes is a conventional method (Tanekawa et al. column 1, lines 25-30). Potman et al. teaches the equivalence of enzymatic degradation of the cell with an exogenous protease and autolysis with the cell's endogenous protease (Potman et al., column 2, lines 45-50).

Response to Applicant's Remarks:

Applicant's Remarks, filed 30 Jan 2009 and 02 Feb 2009, have been fully considered and found not to be persuasive.

The response to Applicant's remarks regarding Tanegawa in view of Keller is as recited above.

Claims 6, 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanekawa et al. (US Patent 4,303,680, issued 1 Dec 1981, of record) in view of Keller et al. (US Patent 4,623,723, issued 18 Nov 1986, of record) as applied to claims 6, 8-11, 13 and 20-29 above, and further in view of Tsuda et al. (US Patent 4,374,981, issued 22 Feb 1983, of record).

Tanekawa et al. in view of Keller et al. render unpatentable a process for producing a flavoring composition containing 5'-ribonucleotides (column 2, lines 9-10) comprising (i) treating yeast cells to release cell contents comprising RNA (Tanekawa et al. column 2, lines 13-16), (ii) separating the RNA present in the released cell contents from other soluble cell material (Keller et al. column 2, lines 58-65), and (iii) converting the separated RNA into 5'-ribonucleotides (Tanekawa et al. column 2, lines 21-25).

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Tanekawa et al. in view of Keller et al. does not disclose the process wherein the 5'-ribonucleotides are further purified by removal of compounds having a higher molecular weight (instant claim 14) by ultrafiltration (instant claim 15).

Tsuda et al. discloses the separation of inosine and/or guanosine by ultrafiltration of fermentation broth to remove high molecular weight substances (Tsuda et al. column 2, lines 9-15). Tsuda et al. teaches ultrafiltration is a useful method to remove both suspended solids and also soluble, high molecular weight contaminants (Tsuda et al. column 1, lines 19-30). Tsuda et al. teaches that ultrafiltration is a useful method for separating inosine and guanosine, useful as starting substances for a flavor nucleotide, from a fermentation broth, or cellular extract, containing such substances (Tsuda et al. column 1, lines 35-39).

It would have been obvious to one of ordinary skill in the art at the time of the invention to improve the invention of Tanekawa et al. in view of Keller et al. by using the known technique of Tsuda et al. to improve a similar method in the same way because of the teaching of Tsuda et al. that ultrafiltration is a useful method to remove both suspended solids and also soluble, high molecular weight contaminants (Tsuda et al. column 1, lines 19-30). Tanekawa et al. discloses a yeast extract containing flavoring nucleotides (Tanekawa et al. column 2, lines 9-10). Tsuda et al. teaches that ultrafiltration is a useful method for separating inosine and guanosine, useful as starting substances for a flavor nucleotide, from a fermentation broth, or cellular extract, containing such substances (Tsuda et al. column 1, lines 35-39). A nucleotide is a nucleoside that is phosphorylated and has a similarly low molecular weight compared to

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high molecular weight contaminants, and with regard to the molecular-weight based filtration methods of Tsuda et al. is a functional equivalent. Therefore to improve the invention of Tanekawa et al. in view of Keller et al. by using the known technique of Tsuda et al. to improve a similar method would have been obvious to one of ordinary skill in the art at the time of the invention.

Response to Applicant's Remarks:

Applicant's Remarks, filed 30 Jan 2009 and 02 Feb 2009, have been fully considered and found not to be persuasive.

The response to Applicant's remarks regarding Tanegawa in view of Keller is as recited above.

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Jonathan Lau Patent Examiner Art Unit 1623 /Shaojia Anna Jiang/ Supervisory Patent Examiner Art Unit 1623